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Petitions Control Branch and
Division of Toxicological Evaluation

October 20, 1966

AF 8-176

Pesticides Branch, Division of Food
Standards and Additives

FAP #6H1946. Synergized pyrethrins in food processing and food storage areas. Evaluation of analytical methods and residue data.

The McLaughlin Gormley King Company proposes a regulation to permit the use of pyrethrins, piperonyl butoxide, and MGK 264 (N-octylbicycloheptene dicarboximide) in food processing and food storage areas with limits of:

1 ppm pyrethrins

10 ppm piperonyl butoxide

10 ppm MGK 264

for residues in milling fractions derived from cereal grains, and with limits of:

3 ppm pyrethrins

10 ppm piperonyl butoxide

10 ppm MGK 264

for residues in other foods.

The use of synergized pyrethrins in food processing and storage areas has been permitted in the past under an extension of the Statute(Sec. 121.91) with tolerances of 3 ppm for pyrethrins and 20 ppm each for piperonyl butoxide and MGK 264. The last extension was granted until 12-31-65.

The petitioner originally requested a permanent regulation in FAP #404 but none was issued because of deficiencies in the pharmacological and analytical data (FSA memo, J. Wolff, 7-29-65). The petition was resubmitted and designated FAP #6H1946.

Conclusions

1. Adequate methods are available, if needed, for enforcement purposes.

2. Residues in foods would not exceed the proposed tolerance levels, if the label directions for the use of synergized pyrethrins sprays in food processing and food storage areas are followed. In the case of pyrethrins a general tolerance of 1 ppm rather than 1 ppm for milling fractions and 3 ppm for other foods would be adequate and more appropriate.

Recommendations

We recommend against establishing the proposed regulation.

Pharmacological considerations permitting, we could recommend that the proposed food additive regulation be established to permit the use of pyrethrins, piperonyl butoxide, and MGK 264 (N-Octylbicycloheptene dicarboximide) in cereal mills, and food processing and food storage areas, with limits of:

1 ppm pyrethrins

10 ppm piperonyl butoxide

10 ppm MGK 264

for residues in all foods.

Our favorable recommendation would be contingent upon the petitioner's revising Label #5 in Sec. B by the addition of a restriction against application to surfaces that may come in contact with food. This conforms with the limitations in the other labels submitted with this petition for similar usages. The regulation should include a statement to the effect that the labelling shall conform to that registered by USDA.

Detailed Considerations

Proposed Use

Pyrethrins, piperonyl butoxide, and MGK 264 are to be used in various spray and aerosol formulations, the maximum concentrations being 0.5% for pyrethrins, 1.0% for piperonyl butoxide, and 1.67% for MGK 264. The remainder of the formulation consists of petroleum distillate, the use of which would be covered by existing Sec. 121.1182 of the food additive regulations.

Space spray formulations are to be used at rates up to 2.6 oz/1000 cu. ft. As a surface spray, applications at the rate of one gallon of the maximum concentration formulation per 1000 sq. ft. are permitted around cracks and crevices in floors, etc. but there is a restriction against treatment of surfaces that may come in contact with food.

Where direct application to food processing equipment is to be made, applications of more dilute sprays are permitted with limitations in the amounts of toxicants per sq. ft. as indicated below.

The pesticides are to be used in areas where food is processed or stored with the following limitations.

1. If the pesticide is to be actually applied directly to food processing or storage equipment the amounts of toxicants per square foot are not to exceed 3 mg pyrethrins, 10 mg piperonyl butoxide and 10 mg MGK 264.

2. Application is not to be made while processing is underway.

3. All food and food processing equipment is to be removed or covered prior to application, or

4. Processing equipment and food handling surfaces are to be thoroughly washed with potable water before processing resumes, or

5. If treated food handling machinery cited in (4) cannot be washed with potable water, a 48-hour delay time between appliation and re-use of the equpment to process food is to be observed.

Label #5 in Sec.B provides for the use of Emulsifiable Synergized Pyrethrins Concentrate in a diluted surface spray in food processing plants. However, this usage could result in residues of pesticides in excess of the permitted amounts listed above. This label should therefore be amended by including a restriction against application to surfaces that may come in contact with food. This would conform with the limitation in the other labels for similar usages.

A statement to the effect that the labelling shall conform to that registered by the USDA would seem appropriate and should be included in the regulation.

Analytical Methods

Several methods of analysis were used for pyrethrins and the synergists, piperonyl butoxide and MGK 264, which utilize colorimetric, GLC, and TLC techniques. The various methods were developed in connection with residue studies on representative commodities including dried fruit, milling products such as flour, and packaged items including "fatty" foods.

The performance of these methods is tabulated below:

Commodity	Method (1)	Blanks (ppm)	% Rec.	Fort. levels (ppm)	Est. Sensit. (ppm)
Pyrethrins					
Dried Fruits	Colorimetric	None reported	99-101	2-4	0.5-1
Flour	ECGC(2)	None reported	94-102	0.05-0.5	0.02
"Fatty" Foods	ECGC(8)	None reported	81-108	0.1-0.5	0.05
Piperonyl Butoxide					
Dried Fruits	Colorimetric(3)	None reported	99-103	4-8	1
Flour	TLC(4)	zero	60-100	0.05-1	0.02
"Fatty" Foods	ECGC(8)	None reported	92-136	0.25-5	0.01
MGK 264					
Dried Fruit	Colorimetric(5)	None reported	102-103	6-12	1.5-3
Warehoused Foods	Colorimetric	<0.05	90-118	0.05-0.2	0.05
Flour	Colorimetric(6)	0.05	Not given(7)	0.05-2	0.05
"Fatty" Foods	ECGC (8)	None reported	93-137	0.4-8	0.01

(1) Schreiber and McClellan, Anal. Chem. 26, 604; 1954.
(2) Donegan et al; Chemistry & Industry; Aug. 1962 (A special detector developed by W.N. Bruce of the Illinois Natural History Survey was used. A paper describing this detector was presented at the ACS meeting in Atlantic City, New Jersey, 9-15-65.)
(3) Jones, JAOAC 35, 771; 1952
(4) Beroza, J. Ag. & Food Chem. 11, 51; 1963. The procedure was quantitized by using a densitometer to compare the intensity of the spots developed with those obtained from standards.
(5) Bruce, unpublished method described in this petition, using ninhydrin as color reagent.
(6) Bruce, unpublished method described in this petition using diazotized 2,4-dinitroaniline as color reagent.
(7) From the O.D. readings reported we would estimate recoveries to be 80% or better.
(8) Same as (2) above, but a special preliminary clean-up using paper chromatography was developed for "fatty foods."

In the case of dried fruits, although more sensitive methods for the determination of the three pesticides would be desirable, we believe these methods are adequate to determine the level of residues to be expected from the described usages. For the other commodities the methods are adequately validated and sufficiently sensitive for use.

To summarize, methods were satisfactorily validated for determining residues of pyrethrins and piperonyl butoxide in dried fruits, flour, and "fatty foods" and for determining MGK 264 in the above commodities as well as in bagged warehouse items such as sugar, beans, and salt. If needed for enforcement purposes the following methods would be satisfactory: for pyrethrins, the ECGC method using the ordinary detector, preceded by paper chromatographic clean-up for fatty foods; for piperonyl butoxide, the colorimetric method based on chromatropic acid see PAM II or ECGC method using the special Bruce detector preceded by the paper chromatographic clean-up for fatty foods; for MGK 264, the colorimetric method of Bruce using diazotized 2,4-dinitroaniline and/or the ECGC procedure using the special detector with the paper chromatographic clean-up for fatty foods.

Since pyrethrins and the synergists are relatively innocuous in nature, a method tryout is not considered necessary.

Residue Data-general

The concentrated sprays (up to 0.5% pyrethrins, 1% piperonyl butoxide and 1.67% MGK 264) to be used mainly in cases where surfaces do not come in contact with food. Provision is also made for uses above covered dried fruit (but not directly to it) and to stored food in multiwall paper bags.

Diluted sprays (0.12% pyrethrins, 0.24% piperonyl butoxide, and 0.4% MGK 264) may be used in institutions, dairies, bakeries, canneries, etc., with restrictions against application directly to food.

Flour and Milling Fractions

Studies were performed to determine the level of residues that might be present from the application of synergized pyrethrins sprays for insect control in cereal grain mills and milled grain products storage areas. Two substrates were used, commercially available baking flour and Pyrax ABB, a finely ground inert diluent having a consistency similar to flour. Pyrax was chosen because pyrethrins and synergists can be extracted without contamination from interfering substances. No data were furnished for milling fractions other than flour, but we would not expect higher residues in these commodities.

Samples of flour and Pyrax were placed in one-gallon glass jars and also in sealed paper bags. Several of the jars were uncovered and several were partially covered. The latter were said to simulate conditions where flour in machinery or chutes might be protected from vertical fallout of the spray, but would be subject to horizontal drift. After treatment, the top 1/2" of sample was collected from the uncovered and partially covered jars and then the next 1" was collected from the uncovered jars. The top 1/4" layer from the paper bags was also collected.

A spray containing 0.4% pyrethrins 0.5% piperonyl butoxide,and 0.5% MGK 264 was used since this formulation is used in large volume in cereal grain mills and product storage areas. A sealed chamber of 100 cu. ft. capacity was used and the chamber remained sealed for 24 hours after treatment. One group of samples received 1 application at 2,4 or 16 fl. oz./1000 cu. ft., another group received two applications, one week apart, at 2 or 4 fl. oz./ 1000 cu. ft.

Residues found in the Pyrax samples were in good agreement with those found in flour.

Residues of pyrethrins were: in the top 1/2" layer of exposed samples, 0.03-0.63 ppm; in the next 1" layer, 0.01-0.21 ppm; in the top 1/2" of partially covered sample, 0.00-0.04 ppm, in the top 1/4" of bagged sample, 0.00-0.06 ppm.

For piperonyl butoxide, corresponding residues were: top layer of exposed, 0.06-0.87 ppm; next layer, 0.02-0.38 ppm; top layer of covered, 0.02-0.08 ppm; top layer of bagged, 0.00-0.03 ppm.

For MGK 264, top layer of exposed, 0.05-0.96 ppm; next layer, 0.02-0.39 ppm; top layer of covered, 0.01-0.10 ppm; top layer of bagged, 0.00-0.05 ppm.

These tests represent treatments at a rate equal to the proposed dosage rate of 2 fl. oz./1000 cu. ft. and at twice and eight times this rate. The portions analyzed represented surface rather than composite residues, and are therefore higher than would be expected to be found in actual practice since mixing occurs in the various processing operations.

Since flour or other milled cereal grain products would be covered before treatment the only residues in these commodities would result from horizontal drift instead of vertical fallout from space or surface applications. These studies indicate such residues would be well below the proposed tolerance levels.

Other Foods

Dried Fruit

A test to determined residues in dried fruit was conducted in a fumigation chamber of 20,000 cu. ft. capacity. The spray formulation contained 0.5% pyrethrins, 1.0% piperonyl butoxide, and 1.67% MGK 264 and was applied 10 times at 2-3 day intervals. The application rate was 1 gal/50,000 cu. ft. or about 2.5 fl oz./1000 cu. ft. Trays of dried apricots, peaches, and pears were placed in random positions seven feet below overhead sprayers. This corresponds to the usage pattern and dosage rate in the labelling in which the overhead spraying of storage areas to control insect for infestations in dried fruit is permitted, except for the restriction against direct application to the fruit, which would require the trays of fruit to be covered.

Residues on the various dried fruits ranged from 0.5-1.9 (av. 1.1) ppm for pyrethrins, 3.7-7.7 (av. 5.2) ppm for piperonyl butoxide, and 1.8-7.2 (av. 4.3) ppm for MGK 264. (No values were obtained for MGK 264 on dried apricots because of interference in the color development).

These results show that even when applications are made to uncovered fruit, residues are well below the proposed tolerances. In the case of pyrethrins the average residue is 1.1 ppm. For covered fruit residues would be much lower. Therefore tolerances of 1,10, and 10 ppm respectively for residues of pyrethrins, piperonyl butoxide and MGK 264 would be adequate.

Packaged Foods Stored in a Warehouse

In the proposed labelling the use of synerized pyrethrins sprays on food stored in multiwall paper bags or cloth bags is permitted. A dosage rate of 1 fl. oz. of spray (0.5% pyrethrins, 1.0% piperonyl butoxide, 1.67% MGK 264) per 1,000 cu. ft. of room space is specified. Repeat applications as necessary for insect control may be made.

Tests to determine residues in packaged foods were made on samples of bagged sugar, dried beans, flour, salt, and brown mustard seed. Five-lb bags of these commodities were placed in the middle of a warehouse floor about 24 feet from a spray dispensing machine. One test reflected application of a spray containing 0.5% pyrethrins, 1.0% piperonyl butoxide, and 1.67% MGK 264 at the proposed rate of 1 fl. oz./1000 cu. ft., the other involving application at 10 times this rate, or 10 fl. oz./1000 cu. ft. Samples were taken for analysis 18 hours after treatment. The bags were carefully cut open and the top $1/2$" of commodity was removed and analyzed for MGK 264.

Residues in the various commodities were; at the rate of 1 fl. oz./1000 cu. ft., 0.00-0.02 ppm and at 10 fl. oz./1000 cu. ft., 0.01-0.15 ppm. Thus no significant residues were found in commodities treated at the proposed dosage rate and only trace residues (<0.15 ppm) in those treated at 10 times the proposed rate.

Since no appreciable amounts of MGK 264 were found in any of the packaged commodities and since MGK 264 is present in the applied formulation in the greatest amount and is a relatively stable compound, we consider it unlikely that residues of the other constituents, piperonyl butoxide or pyrethrins, would be found. (No analyses were made for the latter materials.) Here too the data indicate that a tolerance of 3 ppm for pyrethrins is higher than that required. A tolerance of 1 ppm for this relatively more toxic component, would be adequate.

"Fatty" Foods

Tests were made on three types of "fatty" foods, namely sliced bacon, margarine and shelled Brazil nuts. These items were selected as representative of the various kinds of foods high in fat content that would be subject to treatment as described in this petition. The samples (sliced bacon, covered with one thickness polyethylene and uncovered, approximately 0.25 lb portions; margarine, in original package of one thickness wax paper and an outer box of heavy waxed paper plus a completely uncovered sample; Brazil nuts, shelled, covered in heavy pliofilm in unbroken original package, plus unwrapped samples spread out in a single layer) were placed on the floor of a room of 6200 cu. ft. capacity at a distance of about 18 feet from the spray dispenser.

The spray contained 0.5% pyrethrins, 1.0% piperonyl butoxide, and 1.67% MGK 264 and was dispensed at two separate dosage rates of 1 and 10 fl. oz./1000 cu. ft. After treatments, the sprays were allowed to settle for a period of $1/2$ hour where the lower dosage rate was used and for 4 hours after the higher dosage application.

The results are tabulated below:

		PPM Found		
Product	Dosage	Pyrethrins	Piperonyl But.	MGK 264
Margarine (wrapped)	1 oz.	0	0	0
Margarine (unwrapped)	1 oz.	0.4	0.8	1.7
Bacon (wrapped)	1 oz.	0	0	0
Bacon (unwrapped)	1 oz.	0.4	1.0	2.6
Nuts(packaged)	1 oz.	0	0	0
Nuts(exposed)	1 oz.	0.5	1.1	2.3
Margarine(wrapped)	10 oz.	0.1	0	0.5
Margarine (unwrapped)	10 oz.	2.7	4.1	7.7
Bacon(wrapped)	10 oz.	0.04	0	0.5
Bacon(unwrapped)	10 oz.	3.1	3.9	9.7
Nuts(packaged)	10 oz.	0	0	0
Nuts(exposed)	10 oz.	4.6	7.6	16.4

As can be seen from the table, maximum residues at the proposed dosage rate of 1 fl. oz./1000 cu. ft. were 0.5 ppm for pyrethrins, 1.1 ppm for piperonyl butoxide, and 2.6 ppm for MGK 264, all of which are well below the proposed tolerance levels. These residues were found, as would be expected, on the exposed commodities. At the dosage rate of 10 fl. oz./1000 cu. ft. or 10 times the proposed rate, residues approached the tolerance levels on unwrapped margarine and bacon and exceeded them on the exposed nuts.

However, residues in the wrapped items were well below the proposed tolerances at both the exaggerated dosage rate and the recommended rate.

Residue Data - Summary

The proposed usages of the synergized pyrethrins sprays do not involve direct application to food since the label directions provide for the covering or removal of food before treatment. We would not therefore expect to find significant residues in treated food items and the data support this.

The data presented do indicate that initial residues on representative commodities(flour, dried fruit and packaged items including those of high fat content) would not approach the proposed tolerance levels.

We therefore conclude that residues of pyrethrins, piperonyl butoxide, and MGK 264 will not exceed the proposed tolerances from the described usages. In the case of pyrethrins, the relatively more toxic spray component, a tolerance of 1 ppm for all foods --the same as that proposed for milling fractions--would be adequate and more appropriate.

Other Considerations

We are dubious of the need for and the practicality of the 48 hour delay period listed in the label for food handling machinery. However, the amounts of these pesticides to be applied to food processing or storage equipment per given area are limited as described in the usage section and residues on food later processed on treated equipment are limited to the proposed tolerance levels. The 48 hour delay period can be considered an additional safety factor in insuring that residues, particularly pyrethrins residues, will not exceed these levels. We are therefore not objecting to the inclusion of this provision in the labelling.

We have considered the possibility of migration of residues from the outer paper wrappings into packaged foods during extended periods of storage involving repeated applications of the pesticides. (This type of migration was discussed in detail in the FSA [G.J. Beusch] memo of January 6, 1966, in FAP #4H1455). Since pyrethrins are unstable the only problem is residues of piperonyl butoxide and MGK 264.

However, residues from migration would be far below those from direct application to exposed food. In the case of flour such application yielded a maximum residue of 0.9 ppm of piperonyl butoxide in the top $1/2$" inch and

even less MGK 264. Exposed fatty foods receiving 10 times the recommended dosage showed residues in excess of the tolerance only in the case of nuts. We therefore conclude that any residues due to migration from the paper residues would not cause the tolerances to be exceeded.

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cc:

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FSA/PB
FAP #404
FAP #4H1455
FAP #6H1946
DFC(Jones)
SCI(Johnson)

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RD/I--JAlpert:GJBeusch